

Dietary intake and cardiovascular risk in children and adolescents after cancer treatment

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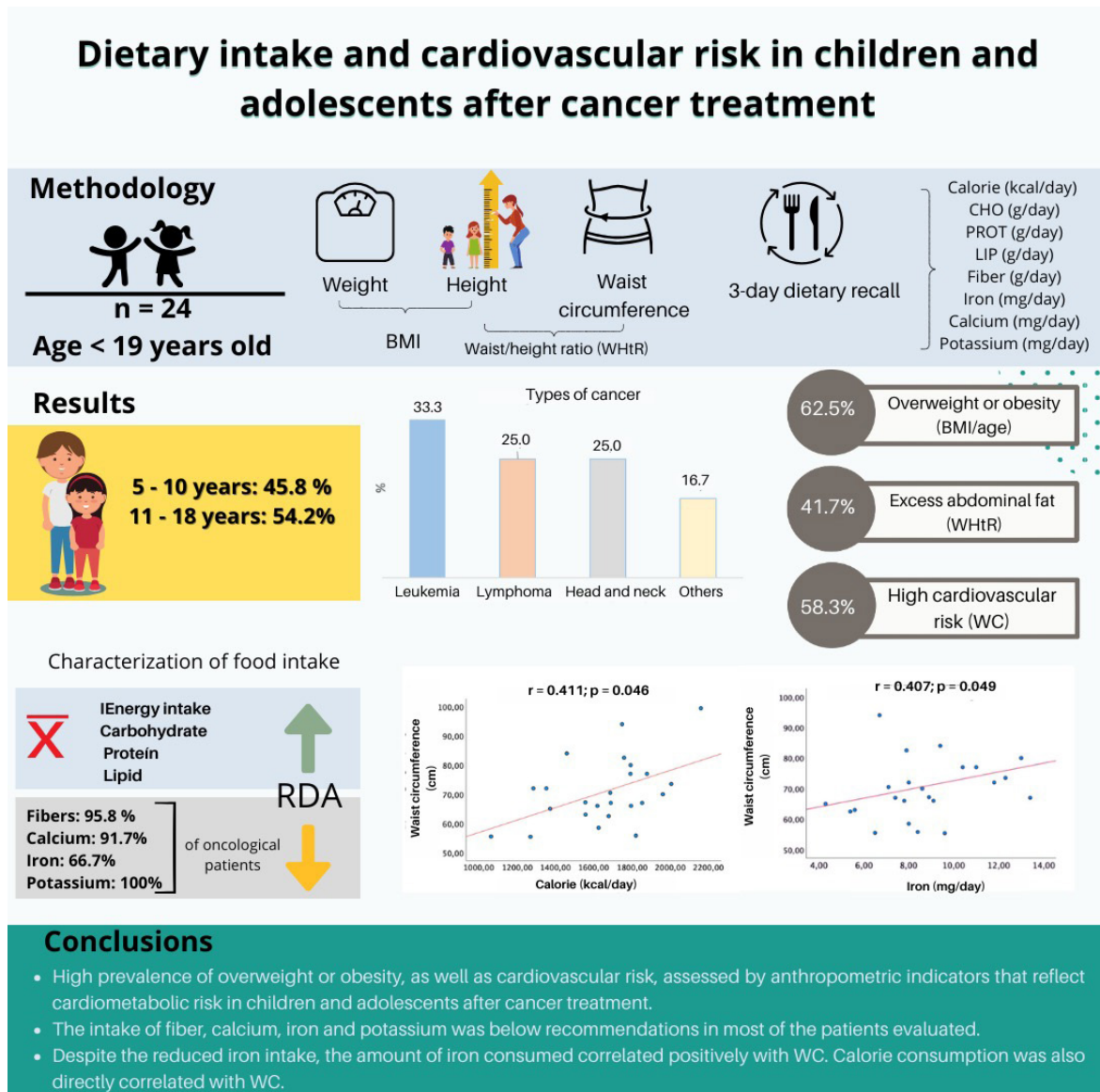
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Graphic Abstract



Abstract

New cancer treatments have increased the life expectancy of children and adolescents, however, they are associated with excess weight and consequently with cardiovascular risk. The objective of this study was to relate dietary intake, cancer remission time with anthropometric indices related to cardiovascular risk in children and adolescents after cancer treatment. A cross-sectional study was carried out with children and adolescents, both sexes, monitored by AVOSOS in the city of Aracaju/SE. The volunteers were evaluated regarding clinical and anthropometric aspects (weight, height, waist circumference [WC], body mass index and waist/height ratio) and food consumption using a 24-hour recall. Pearson or Spearman correlation tests were applied, with $p < 0.05$ being significant. 24 individuals were evaluated (45.8% children and 54.2% adolescents), mean age of 11.6 ± 0.84 years and disease remission time of 26.2 months. The types of cancers reported were leukemia, head and neck, lymphoma and other types (33.3%, 25.0%, 25.0% and 16.7%, respectively). Excess weight/obesity, abdominal fat and increased risk for cardiovascular disease were observed in 62.5%, 41.7% and 58.3% of the sample. The majority of participants had insufficient intake of fiber (95.8%), calcium (91.7%), iron (66.7%) and potassium (100%). A positive correlation was observed between WC and calories consumed ($r=0.411$, $p=0.046$) and dietary iron ($r=0.407$, $p=0.049$). The other variables analyzed were not correlated. Children and adolescents who survive cancer have an increased cardiovascular risk and a positive correlation between WC and caloric intake and dietary iron.

Keywords: Nutritional Status. Anthropometry. Obesity. Children. Teenagers.

INTRODUCTION

The survival rate of patients with childhood cancer has increased, according to data from the American Cancer Society, which show that 85% of patients with childhood cancer have a life expectancy of five years or more, a fact attributed to advances in disease treatment¹. Despite the increase in life expectancy in children after cancer treatment, complications have been observed in this population, among which endocrine complications stand out, which contribute to the development of obesity and the consequent increase in the cardiovascular risk of children after cancer remission².

Post-cancer treatment complications vary depending on the therapy offered and the location of the tumor. In this sense, radiotherapy presents itself as a treatment with the greatest potential risk of contributing to the appearance of endocrine complications. For example, weight gain, increased waist circumference and Body Mass Index (BMI) have been observed in children and adolescents, accompanied by changes in the lipid profile and markers of glycemic control after six months of cancer treatment³.

Furthermore, the treatment of cancers located in the central nervous system causes a reduction in the secretion of pituitary hormones, causing deficiencies in growth hormones (GH), luteinizing hormones (LH), and follicle-stimulating hormones (FSH), thyroid-stimulating hormone (TSH) and adrenocorticotrophic hormone (ACTH), which are associated with an increased risk of developing obesity, diabetes and precocious puberty in children after cancer treatment². In addition to the effects of treatment and type of cancer, lifestyle, such as unhealthy food choices and a sedentary lifestyle, also contributes to obesity in childhood cancer survivors⁴.

Therefore, this study sought to test the hypothesis that diet and cancer remission time are related to increased cardiovascular risk in children and adolescents post-treatment for the disease. Studies of this nature are necessary to better elucidate the factors that contribute to the increase in cardiovascular risk in this population. Therefore, our objective was to relate dietary intake, cancer remission time with anthropometric indices related to cardiovascular risk in children and adolescents after cancer treatment.

METHODOLOGY

Casuistry

A cross-sectional study was carried out, in a convenience sample composed of 24 individuals (children and adolescents) post-cancer treatment, of both sexes, accompanied by the Association of Volunteers at the Service of Oncology in Sergipe (AVOSOS) in the city from Aracaju/SE. Clinical, socioeconomic data, family history of chronic non-communicable diseases, use of medication, presence of associated diseases, practice of physical activity and time of disease remission were obtained, which was self-declared by parents or guardians regarding the last cycle of chemotherapy, the starting from the application of a previously structured form. Participants were also assessed regarding anthropometric characteristics (weight, height and waist circumference) and food intake.

Inclusion criteria were considered: being a resident of the state of Sergipe, being under 19 years old and being monitored for up to five years after remission of the disease. Patients who were using corticosteroids six months or less before the evaluation were excluded.

All those responsible were informed about the procedures to which they would be subjected and signed the Free and Informed Consent Form. This research was approved by the Research Ethics Committee of the Federal University of Sergipe – UFS under nº 1,058,904.

Anthropometric assessment and prediction of cardiovascular risk

Weight and height values, waist circumference were obtained, and the Body Mass Index (BMI) was calculated. Weight, height and waist circumference (WC) values were obtained using the techniques recommended by the Manual of Guidelines for Collec-

tion and Analysis of anthropometric data in health services⁵.

Data on weight, height, WC and BMI were used for nutritional diagnosis by calculating BMI/Age indexes (BMI/A)⁶ and for assessing cardiovascular risk using the ratio of waist measurement to height (WHtR)^{7,8}.

They were considered overweight when the BMI/A ratio was above one standard deviation of the Z-score⁶. Abdominal obesity was considered when WC values were above 90 percent⁹. WHtR greater than or equal to 0.50 was considered excess abdominal fat and high metabolic and cardiovascular risk^{7,8}.

Assessment of dietary intake

To assess dietary intake, the 24-hour dietary recall (24HR) was applied on three non-consecutive days, one day on the weekend, with those over 15 years of age, and with those responsible when the participants were under the age of 15 years.

The analysis of the foods consumed by the research participants was carried out using the NutWin software, from the IT Department of the Escola Paulista de Medicina/UNIFESP. The adequacy of the diet was carried out based on comparisons with the Dietary Reference Intakes proposed by the Institute of Medicine¹⁰⁻¹³.

Statistical analysis

Descriptive analysis of the data was carried out. Continuous data were presented as mean and standard deviation and categorical variables as absolute (n) and relative frequency (%). The Shapiro-Wilk test was applied to evaluate data distribution.

To evaluate the relationship between dietary intake, disease remission time, anthropo-

metric variables and cardiovascular risk predictor indices (WHtR and WC), Pearson and Spearman correlation tests were applied. The correlation was considered weak for r values between 0.10 and 0.29; $r \geq 0.30$ to 0.49 moderate correlation

and $r \geq 0.50$ strong correlation¹⁴.

The collected data were stored in a Microsoft Office Excel 2010 spreadsheet and evaluated using SPSS Software, version 28. P-value < 0.05 was considered significant.

RESULTS

24 patients participated in this study with a mean age of 11.7 ± 0.8 years, of both sexes, with a predominance of females (54.2%). The majority of participants did not practice physical activity (58.3%) and had a family income between one and two minimum wages (75.0%). The average time of disease remission was 26.2 ± 16.6 months. The types of cancers reported were leukemia (33.3%), head and neck cancer (25.0%), lympho-

ma (25.0%), and other cancers (16.7%).

Of the individuals evaluated, 62.5%, 41.7% and 58.3% were overweight or obese according to the BMI/age relationship, excess abdominal fat according to WHtR and high cardiovascular risk according to WC, respectively. Table 1 shows the socioeconomic and anthropometric characteristics of the children and adolescents evaluated.

Table 1 - Clinical, anthropometric and socioeconomic characteristics of children and adolescents post-cancer treatment (Aracaju-SE. 2015).

Variable	N=24	Variable	N=24
Sex, n (%)		Lymphoma	6 (25.0)
Male	11 (45.8)	Other types of cancer	4 (16.7)
Female	13 (54.2)	Weight (kg)	45.1 ± 3.5*
Age (years)	11.6 ± 0.8*	Height (cm)	139.8 ± 7.1*
5 to 10 years old, n (%)	11 (45.8)	Low height for age, n (%)	7 (29.2)
11 to 18 years old, n (%)	13 (54.2)	Appropriate height for age, n (%)	17 (70.8)
Physical activity, n (%)		WC (cm)	70.9 ± 2.3*
Yes	10 (41.7)	No cardiovascular risk, n (%)	10 (41.7)
No	14 (58.3)	Risk associated with obesity, n (%)	14 (58.3)
Family income, n (%)		WHtR, n (%)	
1 to 2 minimum wages	18 (75.0)	No excess of abdominal fat	14 (58.3)
> 2 minimum wages	6 (25.0)	Excess of abdominal fat	10 (41.7)
Disease remission time (months)	26.2 ± 16.6*	BMI (kg/m²) / age relation	21.1 ± 1.1*
0 to 12 months, n (%)	7 (29.2)	Low weight, n (%)	4 (16.7)
13 to 36 months, n (%)	12 (50.0)	Appropriate, n (%)	5 (20.8)
37 to 60 months, n (%)	5 (20.8)	Overweight or obesity, n (%)	15 (62.5)
Types of Cancer, n (%)			
Leukemia	8 (33.3)		
Head and neck	6 (25.0)		

* Data presented as mean and standard deviation.

Data presented in absolute and relative frequency [n (%)].

Caption: BMI: Body Mass Index; WC: Waist Circumference, WHtR: waist/height ratio.

The average caloric, carbohydrate, protein and lipid intake was higher than recommendations, and fiber and calcium intake was lower than recommended by the Institute of Medicine; 91.7% of patients in post-oncological treatment were ingesting calcium below the recommendations for their age, in addition to fiber (95.8%), iron (66.7%) and potassium (100%) below those recommended by DRI according with sex and age. Table 2 presents the characteristics of food

intake of the individuals evaluated.

A positive and moderate correlation was observed between WC values and calorie intake ($r = 0.411$, $p = 0.046$) and iron intake ($r = 0.407$, $p = 0.049$). Dietary intake did not correlate with WHtR and disease remission time, as well as with other variables. Table 3 shows the correlations between dietary intake variables, disease remission time and anthropometric indices that predict increased cardiovascular risk.

Table 2 - Food intake of children and adolescents after cancer treatment (Aracaju-SE. 2015).

Nutrients	Overall (n = 24)	Children (n = 11)	Adolescents (n = 13)	Requirements
Calorie (kcal/day)	1658.2 ± 258.4	1605.0 ± 284.3	1703.2 ± 236.2	-
Carbohydrate (g)	176.9 ± 29.9	17.0 ± 37.2	182.0 ± 2.3	100 g/day
Lipid (g)	77.4 ± 17.6	75.1 ± 18.4	79.3 ± 17.4	ND
Protein (g)	66.3 ± 12.9	70.1 ± 12.1	63.1 ± 13.2	5 – 8 years old: 19 g/day 9 – 13 years old: 34 g/day 14 – 18 years old: Boys: 52 g/day Girls: 46 g/day
Protein (g/kg weight/day)	1.7 ± 0.8	2.4 ± 0.6	1.1 ± 0.3	-
Fiber (g/day)	16.3 ± 4.6	17.5 ± 5.4	15.3 ± 3.7	5 – 8 years old: 25 g/day 9 – 13 years old: Boys: 31 g/day Girls: 26 g/day 14 – 18 years old: Boys: 38 g/day Girls: 26 g/day
Calcium (mg/day)	795.3 ± 184.4	742.4 ± 185.5	840.1 ± 178.1	4 to 8 years old: 1000 mg/day 9 to 13 years old: 1300 mg/day 14 to 18 years old: 1300 mg/day
Iron (mg/day)	8.8 ± 2.4	8.0 ± 2.2	9.4 ± 2.4	4 a 8 anos: 10 mg/dia 9 a 13 anos: 8 mg/dia 14 a 18 anos: Meninos: 11 mg/dia Meninas: 15 mg/dia
Potassium (g/day)	0.9 ± 0.2	0.8 ± 0.2	0.9 ± 0.2	4 to 8 years old: 2.3 g/day 9 to 13 years old: Boys: 2.5 g/day Girls: 2.3 g/day 14 to 18 years old: Boys: 3.0 g/day Girls: 2.3 g/day

Data are presented as mean and standard deviation (SD). Abbreviations: ND: Not determined.

Table 3 - Correlation between dietary intake, cancer remission time and anthropometric variables that predict cardiovascular risk in children and adolescents post-cancer treatment.

Variable	Age (years)*		Height (cm)*		Weight (kg)		BMI (kg/m ²)		WC (cm)		WHtR		Cancer remission time (months)	
	r	P-value	r	P-value	r	P-value	r	P-value	r	P-value	r	P-value	r	P-value
Calorie (kcal/day)	0.287	0.174	0.303	0.150	0.375	0.071	0.324	0.122	0.411	0.046*	0.205	0.336	-0.073	0.735
PTN (g/day)	-0.161	0.452	-0.068	0.753	-0.147	0.494	-0.139	0.517	-0.016	0.940	0.050	0.816	-0.079	0.714
CHO (g/day)*	0.161	0.452	0.286	0.176	0.150	0.583	-0.014	0.947	0.202	0.344	0.020	0.924	-0.122	0.602
LIP (g/day)	0.358	0.086	0.356	0.088	0.285	0.177	0.216	0.310	0.276	0.192	0.037	0.862	-0.103	0.634
Fiber (g/day)	-0.256	0.227	-0.104	0.628	-0.168	0.433	-0.264	0.212	-0.121	0.573	-0.027	0.900	-0.180	0.401
Iron (mg/day)	0.251	0.237	0.189	0.376	0.350	0.094	0.378	0.069	0.407	0.049*	0.140	0.514	-0.310	0.141
Calcium (mg/day)*	0.118	0.583	0.098	0.648	0.192	0.369	0.270	0.202	0.122	0.570	-0.108	0.614	0.012	0.954
Potassium (mg/day)	-0.076	0.723	0.088	0.681	0.103	0.630	0.019	0.929	0.125	0.561	0.001	0.965	0.042	0.845

*Significant P<0.05; Pearson Correlation Test; †Spearman correlation.

Caption: r, correlation coefficient; BMI, body mass index; WC, waist circumference; WHtR, waist-to-height ratio; PTN, protein; CHO, carbohydrates; LIP, lipids.

DISCUSSION

Excess body weight, accumulation of fat in the abdominal region and increased risk of cardiovascular disease were observed in children and adolescents following cancer treatment in the present study. Daily energy intake contributed to the increase in WC, characterized by the intake of carbohydrates, proteins and lipids above those recommended by the DRI. However, it was not possible to establish a correlation between the predictive indices of increased cardiovascular risk with the time of cancer remission in children after treatment of the disease, showing a greater relationship between the increased cardiovascular risk in children after cancer treatment and habits of life. It should be noted that these results are part of a non-probabilistic sample and the sample size does not allow extrapolation of the data.

With the improvement of therapies applied

to cancer treatment, the survival rate of patients with childhood cancer has increased^{3,15}. As a consequence, complications resulting from treatment began to occur more significantly⁴. Obesity is among the most frequent complications after cancer treatment, associated with the use of high doses of corticosteroids, unhealthy food choices and reduced physical activity^{2,4,16}. Similar to our findings, excess weight was observed in 38.8%¹⁷ and 38.2%¹⁸ of Acute Lymphoid Leukemia (ALL) survivors. In our study, it was ensured that corticosteroids had not been used for at least six months before the evaluation, which shows excess weight and fat accumulation in the abdominal region in children and adolescents after cancer treatment regardless of the use of this type of medication.

In the present study, a moderate and direct correlation was observed between the

calories consumed daily and the increase in WC. Furthermore, despite adequate intake of the evaluated macronutrients, the average daily fiber intake was lower than recommended by the Institute of Medicine. The association between inadequate fiber intake and increased body weight has already been observed and is explained, among other factors, by the role of fiber in controlling the intestinal absorption of fats, in managing intestinal transit control and in modulating the intestinal microbiota, in addition to contributing to satiety¹⁹.

The eating habits of children and adolescents under the age of 18 were evaluated in a systematic review that included cohort and observational studies carried out in European, American and Asian countries, observing that Western eating patterns called snack diets, protein/ fiber and those based on sweets increased the chance of children and adolescents being overweight and/or obese²⁰. Furthermore, analyzing data from the China Health and Nutrition Survey (CHNS), three dietary patterns were identified in children and adolescents, categorized into modern and traditional patterns from the north and south, in which the highest quartile of the traditional pattern characterized by milk, fast food, eggs, other meat, poultry and cakes and adopted mainly by younger children and residents in urban areas was associated with overweight and obesity, being explained by the higher intake of calories, carbohydrates, proteins, lipids, fiber, vitamin C, vitamin A, calcium, iron, in the same quartile of the standard, when compared to the other quartiles²¹.

Iron intake in the evaluated population correlated with higher WC. One of the explanations for the relationship between iron and obesity/overweight is due to the interaction between adipose tissue metabolism

and iron regulation, as this mineral acts in the regulation of lipid and glucose metabolism^{22,23}. Changes in the metabolism of these nutrients can contribute to the accumulation of fat in the abdominal region^{22,23}. Most studies do not relate iron intake with markers of cardiovascular risk, but rather indicators of circulating iron status with variables of cardiometabolic risk, especially when the concentration of this mineral is high in the circulation^{24,25}. It should be noted that the public evaluated in the studies is different from that evaluated in this work.

Studies that evaluated the dietary intake of children and adolescents post-cancer treatment are scarce in the literature, however, the results reported in this study are corroborated by a study carried out in Brazil that showed excessive consumption of energy-dense foods, rich in fat, simple sugars and reduced consumption of fiber-rich foods in children and adolescents with cancer²⁶. Complementing the finding, inadequate lifestyle habits such as prolonged exposure to screens, sedentary lifestyle and increased fat intake to the detriment of micronutrient intake were also observed in children with cancer, which increases the percentage of fat mass in this population¹⁶. Furthermore, it was observed that the children and adolescents evaluated had adequate height despite being overweight for their age, contrary to findings in other studies that showed children with short stature and excess body weight²⁷⁻²⁹.

In our study, no correlation was found between the time of disease remission and increased cardiovascular risk, however, a high prevalence of children and adolescents with high waist circumference and WHtR was observed, which denotes an increased risk for cardiovascular diseases. Additionally, daily energy intake was positively correlated with the WC of the po-

pulation evaluated, showing the role of food in increasing cardiovascular risk in this population. It is worth mentioning that the indices used to assess cardiovascular risk reflect the accumulation of fat in the abdominal region and present good performance for assessing cardiovascular risk³⁰, and the findings reported in our study are also in line with those found by Oliveira *et al.*²⁸, who observed 16.1% and 35.5% of abdominal obesity in cancer patients when evaluated by WC and WHtR, respectively.

In addition to lifestyle characteristics such as dietary intake and sedentary lifestyle contributing to obesity, patients undergoing cancer post-treatment, specifically, the type of treatment can contribute to the accumulation of body fat in these patients⁴. Furthermore, corticosteroids used in treatment also play an important role in regulating energy intake, storage and mobilization³¹.

Therefore, considering that factors such

as the type of treatment and type of cancer contribute to obesity and increase the cardiovascular risk of children and adolescents, modifiable factors such as eating habits and physical exercise need to be considered as contributors to the reduction of obesity and cardiovascular risk in this population.

The limitations of this study include the number of participants, which may reduce statistical power, in addition to the lack of information about the medications used during cancer treatment, including dose and duration of use. However, the study provides results that highlight the importance of carrying out prospective studies that evaluate the effects of cancer treatment on excess weight after treatment at different time intervals (short, medium and long term), taking into account food consumption. as one of the factors associated with the development of obesity and related comorbidities.

CONCLUSION

The study showed a high prevalence of overweight or obesity, as well as cardiovascular risk, assessed by anthropometric indicators that reflect cardiometabolic risk. The intake of fiber, calcium, iron and potassium was below recommended in most of the patients evaluated. The time after disease remission did not correlate with the variables of nutrient intake and markers of cardiovascular risk in children and adolescents after cancer treatment. Despite the reduced iron

intake, the amount of iron consumed correlated positively with WC. Likewise, calorie consumption was also correlated with WC.

Therefore, our results highlight the importance of evaluating and monitoring the nutritional status of children and adolescents who have undergone cancer treatment, given the potential of this type of treatment to promote endocrine and metabolic changes, thus increasing cardiovascular risk in this population.

CRedit author statement

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All authors have read and agreed with the published version of the manuscript.

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